

**Pediatric  
Formulation  
Development:  
Challenges of**

**Today and  
Strategies for  
Tomorrow**

*Break-Out Session 3:  
Dosing/Device*

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## Break-Out Session 3: Dosing Device

- These are steering ideas to get participants to think about the subject before the workshop.
- Topics may shift when the workshop approaches however the themes will remain around solid and liquid dosing devices.
- Two main themes are being developed:
  - Dosing devices for multiparticulates and mini-tablets.
  - Administration of small volume oral liquids.

## Solid Oral Dosing Devices

- Several dosing devices are beginning to emerge in the area of mini-tablets ( $> 1$  mm to  $< 4$  mm) and multiparticulates ( $< 1$  mm).
- Strickley provides a review of commercially available pediatric oral formulations since 2007 and highlights some of these devices.
- Even with advancements being made, to the knowledge of the planning committee, no commercial products have been bought forward using such devices.
- Some devices of interest include:

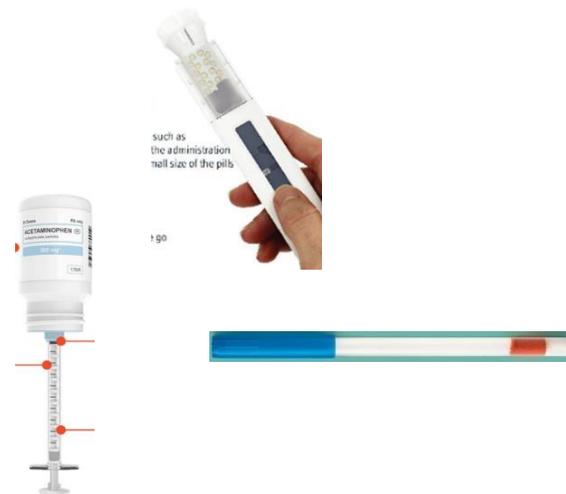
### Mini-tablets

- [sMTS](#) by Balda
- [IQDose](#) by Stiplastics



### Multiparticulates

- [Symphony](#)<sup>TM</sup> by hsd
- [XStraw](#)<sup>®</sup> by DS Technology



## Solid Oral Dosing Devices

- These devices may offer advantages in terms of manufacturability and usability compared to precedented standards.
- Mini-tablets and multiparticulates have relied on the use of single dose technologies such as sprinkle capsules and sachets or scoops/spoons. Some shortfalls of these approaches include:

### **Manufacturability**

- Often times these approaches result in the manufacturing of multiple dose strength capsules or sachets to meet dosing needs.

### **Usability**

- Patients may need to combine together multiple single dose formulations to achieve their intended dose.
- With mini-tablets, as count number becomes larger, controls need to be implemented to ensure patient receives the correct dose.
- New devices offer a promising advancement in the area of dosing of flexible oral solids, but how close are they to commercialization?

## Solid Oral Dosing Devices: **Starter Questions**

- 1) Other than devices highlighted in the pre-read material, are participants aware of any other devices that are well progressed into development towards commercialization?
- 2) How are flexible oral solids currently dosed to patients and why have these administration methods been advocated (i.e. dosing vehicles, soft foods)?
- 3) For mini-tablets, at what unit count do companies consider control methods (i.e. means for count verification) to be required and why?
  - Other than count verification, what are the drivers to move to mini-tablet device over conventional approaches?
  - If a mini-tablet dispenser were utilized what might patient dosing look like?
  - Given training requirements for devices, what are thoughts on their use for acute vs. chronic dosing?

## Solid Oral Dosing Devices: References

Strickley, R.G., Pediatric Oral Formulations: An Updated Review of Commercially Available Pediatric Oral Formulations Since 2007, *J Pharm Sci.* **108** (2019), 1335-1365.

[Furin et al Novel pediatric delivery systems for second-line anti-tuberculosis medications: a case study Int J Tuberc Lung Dis \(2013\) 17:1239](#)

Merck (Andrew Farrington) presented a prototype mini-tablet spoon device at the 2017 EuPFI conference.

## Administration of Small Volume Oral Liquids: **Starter Thoughts**

- Challenges associated with the development and use of administration devices for oral liquids was discussed at EuPFI 2018 [Device workshop](#) and [10<sup>th</sup> EuPFI conference](#).
- An area of concern regarding oral syringes is around accuracy of dosing small volumes and the use of enteral accessories (e.g. straws).
  - [UCL link](#)
  - [BMJ article](#)
- How do you determine and address acceptable dose volumes for oral liquid paediatric medicines (wide age range from neonates upwards, more than one drug product concentration, testing and recommending different syringe sizes)?
- It has been reported that hospital healthcare professionals discard oral devices provided with the product and just use “generic” versions which have not been tested with the product.
  - Potentially lead to issues in dosing accuracy and a lot of waste ([Report](#)).
- A straw-poll conducted by EuPFI industry members on the co-packaging of administration devices found that participants considered the current EU and US regulations to be confusing and inconsistent. They felt it was hard to balance commercial vs. patient needs (cost of developing and testing a device for a product vs. providing a device to the patient that has been tested etc.).
  - Do companies develop a bespoke device or not, and how the decision is made?
- Is the marketing of an oral liquid product without providing syringes a better approach? This will reduce design control requirements but will require testing of multiple off-the shelf syringes. In this case, how many off-the shelf syringes will need to be tested? Any examples? Which standards (if any) do companies test their oral dosing devices against? [There is no ISO standard for oral or enteral syringes].

## Administration of Small Volume Oral Liquids: References

Walsh, J., Math C-M., Breitzkreutz, J., Zerback, T., Wachtel, H., Devices For Oral and Respiratory Paediatric Medicines: What do Healthcare Professionals Think?, *Int J Pharm.* **492** (2015), 304-315. (Includes useful references)

[Johnson & Meyers, Evaluation of Measuring Devices Packaged With Prescription Oral Liquid Medications. J Pediatr Pharmacol Ther \(2016\) 21:75](#)

[Honey et al. Evaluation of oral medication delivery devices provided by community pharmacies. Clin Pediatr \(2013\) 52:418](#)

[Arenas-Lopez et al. Accuracy of enteral syringes with commonly prescribed paediatric liquid medicines. Arch Dis Child \(2017\) 102](#)

[EU Q&A on graduations of oral liquid devices and small volumes](#)